

1. (Amended) A method for identifying a subunit specific modulator of the N-methyl-D-aspartate (NMDA) receptor, comprising:

- C3
- a) providing a plurality of recombinant NMDA receptors which differ in their subunit identity;
 - b) contacting the NMDA receptors of step a) with a neurotransmitter recognition site ligand in the presence and absence of a candidate modulator, wherein the candidate modulator is a steroid-based molecule; and
 - c) assaying for receptor activity following step b), wherein an increase or decrease in activity in at least one, but not all members of the plurality of NMDA receptors, in the presence but not the absence of a candidate modulator, is an indication that the candidate modulator is a subunit specific modulator.

2. (Amended) The method of Claim 1 further comprising comparing the subunit identity of the at least one NMDA receptor whose activity is increased or decreased to the members of the plurality of NMDA receptors whose activity is not increased or decreased to determine the subunit specificity of the candidate modulator.

3. (Reiterated) The method of Claim 1 wherein the plurality of NMDA receptors have identical NR2 subunits, and differ in their NR1 subunits.

4. (Reiterated) The method of Claim 3 wherein the identical NR2 subunits are selected from the group consisting of NR2A, NR2B, NR2C, and NR2D.

5. (Reiterated) The method of Claim 3 wherein at least one of the NR1 subunits is a natural isoform selected from the group consisting of NR1₀₀₀, NR1₀₀₁, NR1₀₁₀, NR1₀₁₁, NR1₁₀₀, NR1₁₀₁, NR1₁₁₀, and NR1₁₁₁.

6. (Reiterated) The method of Claim 3 wherein at least one of the NR1 subunits contain an α exon encoded protein domain.

7. (Reiterated) The method of Claim 3 wherein at least one of the NR1 subunits is a chimeric isoform.

8. (Reiterated) The method of Claim 3 wherein at least one of the NR1 subunits is an isoform point mutant.

9. (Reiterated) The method of Claim 8 wherein the point mutant contains at least one point mutation at a residue which corresponds to residue 182, 193, 202, 233, or 252 of NR1011.

10. (Reiterated) The method of Claim 9 wherein the isoform point mutant is a pentamutant with the amino acid substitution mutations which correspond to mutations R182A, K193A, K202A, R233A, and R252A of NR1011.

11. (Reiterated) The method of Claim 8 wherein the isoform point mutant contains an α exon encoded protein domain and has point mutations within that domain.

26. (Reiterated) The method of Claim 1 wherein assaying step c) is with an oocyte expression system.

27. (Reiterated) The method of Claim 1 wherein the neurotransmitter recognition site ligand is an agonist.

28. (Reiterated) The method of Claim 27 wherein the agonist is selected from the group consisting of NMDA, glutamate, and glycine.

29. (Reiterated) The method of Claim 1 wherein the neurotransmitter recognition site ligand is an antagonist.

32. (Reiterated) The method of Claim 1 wherein the candidate modulator is obtained from a library of small molecules.

33. (Reiterated) The method of Claim 1 wherein the candidate modulator is a known neuromodulator.

Please add new claims 58-65.

C4 -- 58. A method for identifying a subunit specific modulator of the N-methyl-D-aspartate (NMDA) receptor, comprising:

- a) providing a plurality of NMDA receptors which differ in their subunit identity;
- b) contacting the NMDA receptors of step a) with a neurotransmitter recognition site ligand in the presence and absence of a candidate modulator obtained from a library of small molecules; and
- c) assaying for receptor activity following step b), wherein an increase or decrease in activity in at least one, but not all members of the plurality of NMDA receptors, in the presence but not the absence of a candidate modulator, is an indication that the candidate modulator is a subunit specific modulator.

59. The method of Claim 58 further comprising comparing the subunit identity of the subset of the NMDA receptors to determine the subunit specificity of the candidate modulator.

60. The method of Claim 58 wherein the plurality of NMDA receptors have identical NR2 subunits, and differ in their NR1 subunits.

61. The method of Claim 58 wherein the identical NR2 subunits are selected from the group consisting of NR2A, NR2B, NR2C, and NR2D.

62. The method of Claim 60 wherein at least one of the NR1 subunits is a natural isoform selected from the group consisting of NR1000, NR1001, NR1010, NR1011, NR1100, NR1101, NR1110, and NR1111.

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63. The method of Claim 60 wherein at least one of the NR1 subunits contain an α exon encoded protein domain.

64. The method of Claim 60 wherein at least one of the NR1 subunits is a chimeric isoform.

65. The method of Claim 60 wherein at least one of the NR1 subunits is an isoform point mutant. --
